DOI: 10.17986/blm.1664
Adli Tıp Bülteni 2023;28(3):319-322

Sevoflurane Intoxication: A Fatal Suicide

Sevofluran İntoksikasyonu: Ölümle Sonuçlanan Bir İntihar Olgusu

Pınar Efeoğlu Özşeker[1], Ebubekir Burak Çelik[2], Durdu Fatma Çam[1], Tuğçe Koca Yavuz[3]

[1]Çukurova University Faculty of Medicine, Department of Forensic Medicine, Adana, Türkiye
[2]Council of Forensic Medicine Adana Group Administration, Adana, Türkiye
[3]Council of Forensic Medicine Kozan Forensic Medicine Branch Office, Adana, Türkiye

ABSTRACT

A fatal suicide of sevoflurane is presented in this report. A 20-year-old female anesthesia technichian student was found dead lying on her back in dormitory room. The crime scene investigator reported that there was a 250 mL bottle labeled "sevorane liquid 100%" on the table. During the autopsy, no traumatic injuries were found that could have caused the death. Histopathological evaluation of internal organs revealed focal areas of atelectasis and congestion in the lungs, autolysis and congestion in the pancreas, and congestion liver, heart, kidney, brain, cerebellum, and brainstem. Screening for drugs and their metabolites was conducted in blood, urine, and internal organs using enzyme immunoassays along with gas chromatography-mass spectrometry (GC/MS). No traces of any substances, including ethanol, were discovered through the toxicological evaluation. Sevoflurane was identified and quantified using headspace gas chromatography, indicating a concentration of 41.0 µg/mL in the blood. This substance was also confirmed in the gastric content through GC/MS analysis. It was reported that the death of the person occurred as a result of ingestion of sevoflurane and accompanying complications.

Keywords: Sevoflurane, volatile anesthetic, suicide, toxicology, forensic medicine

ÖZ

Bu çalışmada, sevofluranla gerçekleştirilen bir intihar olgu sunulmaktadır. Yirmi yaşında kadın anestezi teknisyenliği öğrencisi, yurt odasında sırt üstü hareketsiz halde ölü olarak bulunmuştur. Olay yeri incelemecisi, masada "sevorane sıvısı %100" olarak etiketlenmiş 250 mL'lik bir şişe olduğunu bildirmiştir. Otopside, ölüme sebep olabilecek travmatik bir lezyon bulunmamıştır. İç organların histopatolojik değerlendirmesinde, akciğerlerde fokal atelektazi ve konjesyon, pankreasta otoliz ve konjesyon, karaciğerde, kalpte, böbrekte, beyinde, beyincikte ve beyin sapında konjesyon gözlenmiştir. Kan, idrar ve iç organlar, enzim immünoanalizleri ve gaz kromatografisi kütle spektrometresi (GC/MS) kullanılarak ilaçlar ve metabolitler açısından taranmıştır. Toksikolojik analizde etanol dahil hiçbir ilaç tespit edilmemiştir. Sevofluran, headspace gaz kromatografisi kullanılarak belirlenmiş ve kandaki konsantrasyonu 41.0 µg/mL saptanmıştır. Ayrıca sevofluran GC/MS ile mide içeriğinde de tespit edilmiştir. Kişinin ölümünün, sevofluranın oral alımı ve beraberinde gelişen komplikasyonlar sonucu meydana geldiği bildirilmiştir.

Anahtar Kelimeler: Sevofluran, volatil anestezik, intihar, toksikoloji, adli tıp

Address for Correspondence/Yazışma Adresi: Tuğçe Koca Yavuz, Council of Forensic Medicine Kozan Forensic Medicine Branch Office, Adana, Türkiye
E-mail: tugcekoca02@gmail.com
ORCID ID: orcid.org/0000-0001-5936-9089

Received/Geliş tarihi: 23.05.2023
Accepted/Kabul tarihi: 28.08.2023

INTRODUCTION

Sevoflurane, a fluorinated inhalation general anesthetic, boasts several characteristics that align with those of an ideal anesthetic. It appears ready to play an increasing role in clinical anesthesia, especially in pediatric anesthesia. This compound was introduced to the field of clinical anesthesia by Maruishi Pharmaceuticals in Japan, before being licensed to Abbott Laboratories in 1996. In Türkiye, Abbott Laboratories markets sevoflurane under the trade name "sevorane" (Figure 1) (1).

Sevoflurane, an anesthetic, appears as a colorless, volatile, and non-flammable liquid possessing an odor reminiscent of ether. Chemically, it's a polyfluorinated methyl-isopropyl compound (Figure 2), boasting a molecular weight of 200 atomic mass units and stability at room temperature. Its boiling point and vapor pressure are noted as 58.6 °C and 157 mmHg respectively. Its noteworthy trait is its blood solubility, evidenced by a blood/gas partition coefficient of 0.69 (2).

In humans, between 2% and 5% of the absorbed sevoflurane dose undergoes metabolic breakdown in the liver. This process leads to the production of inorganic fluoride and the organic fluoride metabolite hexafluoroisopropanol, which is then conjugated with glucuronic acid and quickly excreted via the kidneys. The cytochrome P450 (CYP)2E1 pathway is primarily involved in this biotransformation (3,4).

Figure 1. An anesthetic inhalant "sevorane"

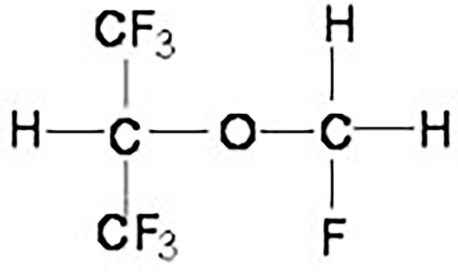

Figure 2. Chemical structure of sevoflurane

While incidents of intoxication related to isoflurane and halatone are documented in literature, cases of Sevoflurane-related fatalities are exceedingly rare (5-8). Notably, the case that will be discussed below, a death due to orally suicidal use of sevoflurane, the first recorded incident of its kind in Türkiye, to the best of our knowledge.

CASE REPORT

A 20-year-old female student anesthesia technician student was found dead in her dormitory room, lying supine. There was a 250 mL bottle labeled "sevorane liquid %100", of which only approximately 15-20 mL of fluid remained.

The hospital records revealed that the decedent had presented to the emergency department the day prior to her death, complaining of syncope and fainting. Routine blood tests and cardiac markers were analyzed, with creatine kinase-MB and troponin levels found to be 0.6 ng/mL and 0.01 ng/mL, respectively. After receiving treatment, the patient was discharged. Notably, her medical history included a leaky heart valve. Upon discovery of the body, it was transported to the Forensic Medicine Council in Adana, where the autopsy was conducted 24 hours after the initial discovery.

The autopsy did not reveal any traumatic injuries that could be identified as the cause of death. Histopathological evaluation of the internal organs noted focal atelectasis and congestion in the lungs, autolysis and congestion in the pancreas, and congestion in the liver, heart, kidneys, brain, cerebellum, and brainstem. For toxicological analysis, samples were taken from various sources (blood, urine, liver, lungs, brain, kidneys, heart, etc.), sealed in vials, and stored at -20 °C.

MATERIALS AND METHODS

A drug abuse screening was performed using enzyme immunoassays to detect substances including amphetamines, barbiturates, cannabinoids, cocaine, methadone, opiates, and phencyclidine. Toxicological drug screening for acidic, basic, and neutral drugs was performed using gas chromatography-mass spectrometry. Volatile substances such as ethanol, methanol, isopropanol, and acetone were screened using headspace/gas chromatography with a flame ionization detector. Given the circumstances surrounding this case, sevoflurane was also included. Sevoflurane was procured from the United States Pharmacopeia Reference Standard (Merck, Darmstadt, Germany), and n-propanol, which was used as an internal standard (IS), was purchased from Merck (Darmstadt, Germany).

Sample Preparation

For the analysis, a 200 µL aliquot of whole blood was combined with 800 µL of an n-propanol IS inside a 20 mL headspace vial. The vial was promptly sealed using a rubber cap and an aluminum crimp to maintain the integrity of the sample.

Then, a 1 mL sample from the headspace of the sealed vial was extracted and directly introduced into the headspace-gas chromatography instrument for further examination.

Instrumentation

Volatile screening was performed on an Agilent 7820 A gas chromatograph equipped with an FID detector (Agilent, USA) and a DB-ALC1 column (30 m × 0.320 mm ID × 1.80 µm) (Agilent J&W, USA). The oven and detector temperatures were set at 40 and 280 °C, respectively. Nitrogen was used as the carrier gas (35 mL/min), and as the detector gas along with hydrogen and air. The analysis was conducted using the Agilent 7694 headspace autosampler. The settings for this process included a sample loop time of 0.05 minutes, an equilibrium time of 5.0 minutes, and an injection time of 0.1 minutes. The temperature program commenced with the oven stabilized at 40 °C, which was maintained for a duration of 5 minutes. Following the run, the post-run time and temperature were set at 4.0 minutes and 180 °C, respectively. The entirety of one temperature cycle was completed in 15 minutes.

RESULTS

Urine screening was negative for the tested drugs of abuse: amphetamines, barbiturates, cannabinoids, cocaine, methadone, opiates, and phencyclidine. No drugs were detected in the blood, urine, liver, lung, kidney, and brain samples. The autopsy results showed no traumatic lesions that could have caused death.

Sevoflurane calibration points were at concentrations of 0.9, 1.8, 3.6, 5.4, 7.2, 9.0, 10.8, and 12.6 mg/dL. N-propanol was used as an IS. Toxicological analysis revealed no alcohol in the blood but did find sevoflurane at a concentration of 41.0 µg/mL (Figure 3). Sevoflurane was also qualitatively detected in the gastric contents.

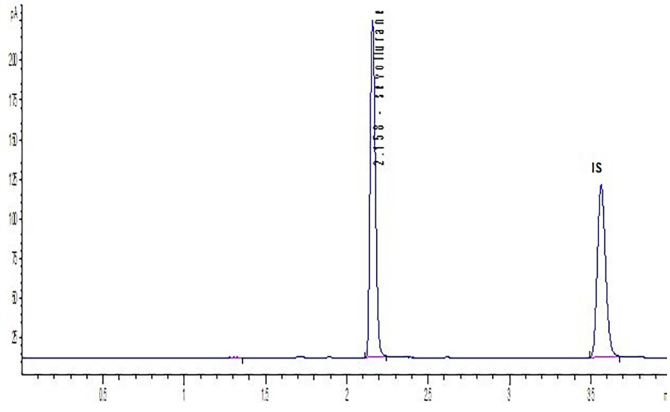

Figure 3. Chromatogram of sevoflurane detected in blood

IS: Internal standard

DISCUSSION

The abuse rate for general inhalation anesthetics is relatively lower compared to other illegal substances, they can be fatal if not properly used (9). The potency of these anesthetics places them amongst the high-risk drugs, given that a mere 2-4 times increase over the therapeutic dose can lead to circulatory failure (10).

Burrows et al. (9) presented an instance of respiratory depression induced by sevoflurane in their case study. The decedent was discovered lifeless on a bed, with an oxygen mask containing a gauze pad fitted over his face. Three used and one full bottle of Ultane® were found alongside the body. The research revealed that, determined by headspace gas chromatography, the concentrations of sevoflurane were as follows: 26.2 µg/mL in the blood, 86.7 µg/mL in vitreous fluid, 31.9 µg/mL in tracheal aspirate, 105 µg/mL in urine, 30.8 mg/kg in the liver, and 12.8 mg/kg in the kidneys. They found at the higher concentrations of sevoflurane in vitreous fluid than in blood. The lack of our study is analyzed of sevoflurane in vitreous fluid. Furthermore, upon postmortem examination of the deceased, indications of respiratory depression were found, including neck vein distension, pulmonary atelectasis, and pulmonary edema (9).

Rosales et al. (11) revealed the concentrations of sevoflurane in blood, brain, and lung following a fatal event caused by the anesthetic. The victim, a 31-year-old male anesthetist, was found deceased in an operation room's break area, prone on a bed and gripping an uncapped empty Ultane® bottle. Autopsy results showed pulmonary edema and lung frothing. The investigation recorded a sevoflurane concentration of 15 mg/mL in the blood and 130 mg/kg in the lungs (11). Interpreting the quantitative results of sevoflurane can be challenging as the blood concentration could be therapeutic or lethal depending on various factors like adequate clinical monitoring (10).

In this particular case, sevoflurane was the only substance detected in the blood and stomach contents. Given this evidence, we believe the cause of death could be ingestion of the substance, not inhalation, aligning with the crime scene findings.

The therapeutic concentration of sevoflurane is 134.0 µg/mL in the literature (12). However, its lethal concentration in the human bloodstream is unknown. A literature study reported a sevoflurane concentration of 41.0 µg/mL in the blood during and post-anesthesia as non-toxic (13). However, the most noteworthy and pertinent observation in sevoflurane poisoning is the drug's ability to reduce peripheral resistance and mean arterial blood pressure. The father of the deceased disclosed that she had a heart valve defect. Considering the sevoflurane-labeled sevorane liquid bottle at the crime scene and the detected presence of sevoflurane in the deceased's blood and stomach content, it was concluded that the death resulted from anesthetic substance overdose and related complications.

To our knowledge, this is the first sevoflurane-related death reported in Türkiye.

Potential abusers of sevoflurane primarily include hospital staff, medical students, and those involved in the production and distribution of these agents. It is crucial to limit access to such volatile anesthetics and enforce restrictive measures on these drugs. For hospital employees, we strongly recommend routine workplace drug testing.

ETHICS

Ethics Committee Approval: In this study, the criteria of the Declaration of Helsinki were taken into consideration.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.B.Ç., Concept: P.E.Ö., D.F.Ç., T.K.Y., Design: P.E.Ö., D.F.Ç., T.K.Y., Data Collection or Processing: P.E.Ö., E.B.Ç., Analysis or Interpretation: P.E.Ö., Literature Search: P.E.Ö., D.F.Ç., T.K.Y., Writing: D.F.Ç., T.K.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Alanoğlu Z, Güçlü Yıldırım C, Bermede AO, Alkış N. What is the Difference Between Different Sevoflurane Products? JARSS. 2012;20(4):189-195. https://anestezidergisi.com/pdfs/2012_4-189-195.pdf
2. Seymour C, Shaner RL, Feyereisen MC, Wharton RE, Kaplan P, Hamelin EI, et al. Determination of fentanyl analog exposure using dried blood spots with LC-MS-MS. J Anal Toxicol. 2019;43(4):266-276. http://doi.org/10.1093/jat/bky096
3. De Hert S, Moerman A. Sevoflurane. F1000Res. 2015;4(F1000 Faculty Rev):626. http://doi.org/10.12688/f1000research.6288.1.
4. Behne M, Wilke HJ, Harder S. Clinical pharmacokinetics of sevoflurane. Clin Pharmacokinet. 1999;36(1):13-26. http://doi.org/10.2165/00003088-199936010-00002
5. Spencer JA, Green NM. Suicide by ingestion of halothane. JAMA. 1968;205(10):702-703. https://pubmed.ncbi.nlm.nih.gov/5695148/
6. Spencer JD, Raasch FO, Trefny FA. Halothane Abuse in Hospital Personnel. Surv Anesthesiol. 1976;20(6):573.
7. Pavlic M, Haidekker A, Grubwieser P, Rabl W. Fatal accident caused by isoflurane abuse. Int J Legal Med. 2002;116(6):357-360. http://doi.org/10.1007/s00414-002-0340-9
8. Levine B, Cox D, Jufer-Phipps RA, Li L, Jacobs A, Fowler D. A fatality from sevoflurane abuse. J Anal Toxicol. 2007;31(8):534-536. http://doi.org/10.1093/jat/31.8.534
9. Burrows DL, Nicolaides A, Stephens GC, Ferslew KE. The distribution of sevoflurane in a sevoflurane induced death. J Forensic Sci. 2004;49(2):394-397. https://pubmed.ncbi.nlm.nih.gov/15027568/
10. Pihlainen K, Ojanperä I. Analytical toxicology of fluorinated inhalation anaesthetics. Forensic Sci Int. 1998;97(2-3):117-133. http://doi.org/10.1016/s0379-0738(98)00148-0.
11. Rosales CM, Young T, Laster MJ, Eger EI 2nd, Garg U. Sevoflurane concentrations in blood, brain, and lung after sevoflurane-induced death. J Forensic Sci. 2007;52(6):1408-1410. http://doi.org/10.1111/j.1556-4029.2007.00556.x
12. Baselt RC. Disposition of Toxic Drugs and Chemicals in Man, 9th ed. Seal Beach, CA, USA: Biomedical Publications; 2011.
13. Biricik E, Karacaer F, Güneş Y, Dağlıoğlu N, Efeoğlu P, Ilgınel M, et al. Effect of One-Lung Ventilation on Blood Sevoflurane and Desflurane Concentrations. J Cardiothorac Vasc Anesth. 2019;33(2):442-449. http://doi.org/10.1053/j.jvca.2018.05.032